Hydroxyapatite Crystals in Tumoral Calcinosis: A Case Report

MASAHITO HATORI¹, KOUICHI OOMAMIUDA² and SHOICHI KOKUBUN¹

¹*Department of Orthopaedic Surgery, Tohoku University School of Medicine, Sendai 980-77, and* ²*Central Research Laboratory, Sumitomo Osaka Cement Co., Ltd, Funabashi 274.*

HATORI, M., OOMAMIUDA, K. and KOKUBUN, S. *Hydroxyapatite Crystals in Tumoral Calcinosis: A Case Report* Tohoku J. Exp. Med., 1996, **180** (4), 359-364
—— Calcified deposits of tumoral calcinosis from a 77-year-old Japanese woman were examined by scanning electron microscopy (SEM) and x-ray diffraction method. SEM revealed conglomerates of granular calcified materials 0.2 to 0.5 μ m in size. X-ray diffraction method revealed the presence of hydroxyapatite that was highly crystallized. No other components such as calcium pyrophosphate dehydrate were detected. ——— tumoral calcinosis; scanning electron microscopy; x-ray diffraction method; hydroxyapatite

Tumoral calcinosis is a rare condition characterized by large calcific masses occurring predominantly in the juxta-articular region of the extremity. There have been few reports of tumoral calcinosis that identified the calcium deposits (Lafferty et al. 1965; Boskey et al. 1983; Slavin et al. 1993; Kokubun et al. 1996). We analyzed the calcified material by using scanning electron microscopy (SEM) and x-ray diffraction.

CASE REPORT

A 77-year-old Japanese woman presented with a mass about her right ilium. It had slowly grown for seven years. She had no history of trauma or other medical illness. Her family history was unremarkable. Physical examination revealed a 3×4 cm hard subcutaneous mass over the right anterior superior iliac spine. The mass was firm and fixed to the underlying tissue. The overlying skin, however, was freely movable and had no redness or heat. Serum calcium and phosphorus levels were within normal limits. Other laboratory data were also noncontributory. A plain radiograph showed a multilobulated calcified mass

Received July 29, 1996; revision accepted for publication November 18, 1996.

Address for reprints: Masahito Hatori, M.D., Department of Orthopaedic Surgery, Tohoku University School of Medicine 1-1 Seiryomachi, Aoba-ku, Sendai 980-77, Japan.

(Fig. 1). The mass was removed en bloc.

Macroscopically, the mass was composed of chalky white materials and well encapsulated (Fig. 2). Microscopically, the mass was circumscribed by thick fibrous tissue and consisted of numerous loculi of various sizes separated by fibrous septa extending inward from the capsule. The loculi contained calcific deposits. Newly formed capillaries and collections of histiocytes and foreign body giant cells were observed underneath the capsule and along the peripheral septa (Fig. 3). Granuli were obtained by fracturing the calcified materials with a small metal blade at the center and periphery portions of the removed mass. They were dried at 50°C, coated with gold and examined with a Nihon Denshi (Tokyo) JSM-5400LV scanning electron microscope operating at an accelerating voltage of 20 kV in order to observe the external aspect of the deposits. Conglomerates of granular crystals with the size of 0.2 to 0.5 μm were observed in all the samples (Fig. 4). Powder x-ray diffraction pattern of the calcified deposits was obtained with a Rigaku (Tokyo) D-MAX-2C diffractometer over the range of $2\theta=5$ to 60 degrees with Cu $K\alpha$ x-rays at 40 kV, 100 mA. This pattern well coincided with that of hydroxyapatite (HA). No other components such as calcium pyrophosphate dehydrate were detected (Fig. 5).

Fig. 1. Radiograph showing a calcified mass close to the anterior superior iliac spine (arrow).

Fig. 2. Cross section revealing a multilocular calcified mass surrounded by dense fibrous tissue.

Fig. 3. Photomicrograph showing islands of calcified deposits and cells (hematoxylin and eosin staining). The scale indicates 100 μm .

Fig. 4. Scanning electron photomicrograph showing conglomerate of granular deposits with the size of 0.2 to 0.5 μm . The scale indicates 1 μm .

Fig. 5. The x-ray diffraction analysis demonstrating that the pattern of this calcified material coincides well with that of high-crystalline hydroxyapatite. (CPS: count per sec, 2θ : diffraction angle)

DISCUSSION

The term tumoral calcinosis was first coined by Inclan et al. in 1943. It is found mainly in the regions of the hip, shoulder, and elbow. It is predominant

in adolescents and young adults, and more often multiple than solitary. Unlike calcification associated with renal insufficiency, hypervitaminosis D, and milk-alkali syndrome, there are no demonstrable abnormalities in calcium metabolism although hyperphosphatemia has been observed in some instances (Lafferty et al. 1965; Berghausen et al. 1987).

The pathogenesis of tumoral calcinosis remains obscure. Trauma is rarely reported by patients with tumoral calcinosis, but minor repeated trauma and tissue injury seem to play a role in the calcifying process (Enzinger and Weiss 1995). In the present case, judging from the location of the anterior superior iliac spine which is known to be liable to pressure, it could be possible that minor trauma triggered a mechanism, beginning with edema and collagenization and ending with collagenolysis and ultimately massive calcification. Such a mechanism was suggested by Thompson and Path (1966). They stated that the pressure of sleeping on hard ground could explain the principal sites of tumoral calcinosis in African blacks.

In most published papers on tumoral calcinosis, precise crystal identification was rare. According to Resnick (1988), the identification of individual HA crystals or of closely related calcium phosphate crystals is generally impossible by light or polarized microscopy owing to their minute sizes. Precise identification requires electron microscopic or radioisotopic techniques or x-ray diffraction analysis. Boskey et al. (1983) used x-ray diffraction which revealed calcium crystals in tumoral calcinosis to be HA. Dryll et al. (1984) determined HA by x-ray microanalysis and electron diffraction. Kokubun et al. (1996) reported a tumoral calcinosis in the spine, consisting of crystals of calcium pyrophosphate dehydrate verified by SEM and energy-dispersive x-ray analysis. In the present case, the results of SEM and the x-ray diffraction led us to the conclusion that the calcified deposits was HA.

Generally, HA in the human body has extremely low crystallinity except for dental enamel. For example, cortical bone or ectopic calcification consists of low crystalline or amorphous HA which has broad peaks on a x-ray diffraction pattern (Hatori et al. 1995). Interestingly, in the three cases of tumoral calcinosis analyzed by Boskey et al. (1983), all of these deposits differed from normal bone mineral, being heavily mineralized and containing larger, more perfect HA crystals. Calcified material sampled in the present case had also sharp peaks indicating highly crystallized HA. Fleish (1991) suggested the inhibition of ectopic mineralization is most probably due to the physicochemical inhibition of crystal growth. Lack of a potent down-regulator of HA crystal formation such as pyrophosphate (Fleisch et al. 1966) could be thought to be one of the causative factors for slow but steady growth of the calcified mass. It deserves further investigation.

Acknowledgments

We thank Osamu Suzuki, Ph.D. for his valuable suggestions and Mr. Katsuyoshi Shoji and Ms. Tomoko Takeda for their technical help.

References

- 1) Berghausen, E.J., Balogh, K., Landis, W.J., Lee, D.D. & Wright, A.M. (1987) Cervical myelopathy attributable to pseudogout: Case report with radiologic, histologic, and crystallographic observations. *Clin. Orthop.*, **214**, 217-221.
 - 2) Boskey, A.L., Vigorita, V.J., Sencer, O., Stuchin, S.A. & Lane, J.M. (1983) Chemical, microscopic, and ultrastructural characterization of the mineral deposits in tumoral calcinosis. *Clin. Orthop.*, **178**, 258-269.
 - 3) Dryll, A., Bardin, T., Lansaman, J., Tran, V.P., Bard, H., Ryckewaert, A. & Cywiner, G.C. (1984) Tumoral calcinosis: Light and electron microscopic study with electron diffraction and x-ray microanalysis of the mineral deposits. *J. Submicrosc. Cytol.*, **16**, 577-583.
 - 4) Enzinger, F.M. & Weiss, S.W. (1995) Tumoral calcinosis. In: *Soft Tissue Tumors*, edited by F.M. Enzinger & S.W. Weiss, Mosby, St. Louis, Baltimore, Berlin, Boston, Carlsbad, Chicago, London, Madrid, Naples, New York, Philadelphia, Sydney, Tokyo, Toronto, pp. 1039-1045.
 - 5) Fleish, H. (1991) Bisphosphonates. Pharmacology and use in the treatment of tumour-induced hypercalcaemic and metastatic bone disease. *Drugs*, **42**, 919-944.
 - 6) Fleisch, H., Russell, R.G.G. & Straumann, F. (1966) Effect of pyrophosphate on hydroxyapatite and its implications in calcium homeostasis. *Nature*, **206**, 901-903.
 - 7) Hatori, M., Sakurai, M., Watanabe, N. & Oomamiuda, K. (1995) Calcific bursitis in a three-year-old boy: A case report. *Foot Ankle Int.*, **16**, 295-298.
 - 8) Inclan, A., Leon, P. & Camejo, M.G. (1943) Tumoral calcinosis. *JAMA*, **121**, 490-495.
 - 9) Kokubun, S., Ozawa, H., Sakurai, M. & Tanaka, Y. (1996) Tumoral calcinosis in the upper cervical spine. A case report. *Spine*, **21**, 249-252.
 - 10) Lafferty, F.W., Reynolds, E.S. & Pearson, O.H. (1965) Tumoral calcinosis. A metabolic disease of obscure etiology. *Am. J. Med.*, **38**, 105-118.
 - 11) Resnick, D. (1988) Calcium hydroxyapatite crystal deposition disease. In: *Diagnosis of Bone and Joint Disorders*, edited by D. Resnick & G. Niwayama, Vol. 2, W.B. Saunders, Philadelphia, pp. 1733-1764.
 - 12) Slavin, R.E., Wen, J., Kumar, D. & Evans, E.B. (1993) Familial tumoral calcinosis. A clinical, histopathologic, and ultrastructural study with an analysis of its calcifying process and pathogenesis. *Am. J. Surg. Pathol.*, **17**, 788-802.
 - 13) Thompson, J.G. & Path, F.C. (1966) Calcifying collagenolysis (tumoral calcinosis). *Br. J. Radiol.*, **39**, 526-532.
-